REMARKS

Reconsideration of the present application is respectfully requested in view of the above amendments and the following remarks. Claims 1-26 are pending in the application; claims 1-13 are currently under examination, and claims 14-26 are withdrawn. Claim 5 has been amended to correct an obvious typographical error. No new matter has been added by this amendment.

CLAIM OBJECTIONS

The Examiner objected to claim 5 for an alleged typographical error in the recitation "arid."

Claim 5 has been amended to recite "and" instead of "arid," thereby correcting the typographical error noted by the Examiner. Applicants, thus, respectfully request withdrawal of this objection.

REJECTIONS UNDER 35 U.S.C. § 102

The Examiner rejected claims 1-13 under 35 U.S.C. § 102(e) for alleged lack of novelty over DeFrees *et al.* (U.S. Patent No. 7,125,843). The Examiner asserts that DeFrees *et al.* teach a conjugate molecule comprising an antibody that is covalently linked to a biologically active polypeptide, such as erythropoietin. The Examiner then asserts that the antibody of DeFrees *et al.* inherently contains an immunoglobulin Fc fragment, and, thus, essentially asserts that the conjugated antibody of this reference falls within the scope of the presently claimed composition.

Applicants traverse this rejection and submit that the instant claims satisfy the requirements of novelty over DeFrees *et al.* Embodiments of the instant claims relate, in pertinent part, to pharmaceutical compositions comprising an immunoglobulin Fc *fragment* as a carrier, wherein said immunoglobulin Fc fragment is covalently linked to a drug that is a physiologically active polypeptide through a *non*-peptide linker.

DeFrees *et al.* fail to disclose each feature of the instant claims. For instance, DeFrees *et al.* not only fail to disclose a composition comprising an Fc *fragment* that is linked to

a polypeptide through a *non*-peptide linker. In this regard, Applicants respectfully disagree with the Examiner's assertion that DeFrees *et al. inherently* disclose the use of an immunoglobulin Fc *fragment*, merely because they disclose a whole *antibody* (*see* the Action, page 3) as one possible component of a conjugate molecule. Instead, as disclosed in the specification, it is respectfully submitted that the antibody-based conjugates of DeFrees *et al.* do not fall within the scope of the instant claims, whether inherently or otherwise.

The immunoglobulin Fc *fragment* of the instant claims represents a structurally distinct molecule as compared to the whole antibody of DeFrees *et al.*, rendering the presently claimed conjugates novel over those of DeFrees *et al.* On this point, Applicants note that an "immunoglobulin Fc *fragment*" is expressly defined in the specification to *exclude* whole antibodies, such as the antibody of DeFrees *et al.* relied upon by the Examiner (*see, e.g.,* page 11, lines 9-15 of the specification). Specifically, the specification states that an "immunoglobulin Fc fragment" does ***not*** contain "the variable regions of the heavy and light chains, the heavy-chain constant region 1 (CH1) and the light-chain constant region 1 (CL1) of the immunoglobulin." *Id.*

In contrast, persons skilled in the art would understand that the antibody of DeFrees *et al.* contains these structural features. Indeed, DeFrees *et al.* expressly define an "antibody" as "an immunoglobulin molecule which is able to *specifically bind to a specific epitope on an antigen*" (*see, e.g.,* column 36, lines 65-37 of DeFrees *et al.*)(emphasis added), in part, because DeFrees *et al.* rely on such functional and inherent structural characteristics in their use of an antibody as a *targeting agent* (*see, e.g.,* column 68, last full paragraph of DeFrees *et al.*). However, as noted above, the immunoglobulin Fc fragments of the instant claims do not contain the structural features required to *specifically bind to a specific epitope on an antigen* (*e.g.,* variable regions), as in DeFrees *et al.*, because the conjugates containing those Fc fragments are used as carriers, not targeting agents. With respect to their function as carriers, Applicants note that the instant immunoglobulin Fc fragments have a relatively low molecular weight as compared to whole immunoglobulin molecules, providing significant advantages in the preparation, purification, and yield of conjugates. Moreover, since the immunoglobulin Fc fragments of the instant claims do not contain Fab fragments, the compositions obtained

therefrom not only have increased homogeneity, but are less antigenic (*see, e.g.,* page 12, lines 13-20 of WO 2005/047336). Therefore, by disclosing a structurally distinct molecule, it is respectfully submitted that DeFrees *et al.* fail to disclose, *inherently* or otherwise, a protein conjugate comprising a physiologically active polypeptide, a non-peptide polymer, and an immunoglobulin Fc fragment, as presently claimed.

While Applicants recognize that the Examiner must give the claims the broadest reasonable interpretation during prosecution, Applicants also respectfully submit that such an interpretation must be *consistent with the specification* and the understanding of a person skilled in the art. *See, e.g., In re Cortwright*, 165 F.3d 1353 (Fed. Cir. 1999). Here, since the specification expressly defines an "immunoglobulin Fc *fragment*" to exclude certain structural features that are inherent in a whole antibody, then it is axiomatic under a section 102 analysis that the instant claims cannot be construed to read on the conjugates of DeFrees *et al.*, wherein those conjugates are limited to whole antibodies, or other "agents" that likewise fail to read on an immunoglobulin Fc *fragment*.

This deficiency of DeFrees *et al.* is especially acute given the further failure of this reference to disclose a conjugate comprising an immunoglobulin Fc *fragment* that is covalently linked to a physiologically active polypeptide through a *non*-peptide linker. Indeed, with regard to Fc fragments, DeFrees *et al.* is limited to fusion proteins comprising Fc fragments (*e.g.,* Enbrel®), necessarily comprising peptide linkers, as opposed to conjugates of Fc fragments that utilize a *non*-peptide linker, as presently claimed. Therefore, DeFrees *et al.* fail to anticipate the instant claims.

Given the failure of DeFrees *et al.* to disclose a conjugate molecule comprising an "immunoglobulin Fc *fragment*," as presently claimed, wherein that Fc fragment is covalently linked to a polypeptide through a *non*-peptide linker, Applicants submit that the instant claims satisfy the requirements of novelty over this reference. Applicants, thus, respectfully request withdrawal of this rejection under 35 U.S.C. § 102(e).

DOUBLE PATENTING REJECTIONS

The Examiner *provisionally* rejected claims 1-13 for alleged nonstatutory obviousness-type double patenting over claims 1-19 and 27-45 of co-pending U.S. Application No. 10/535,232. The Examiner recognizes that these claims are not identical, but asserts that they are directed to nearly the same polypeptide conjugates and compositions.

Applicants traverse this rejection. Nonetheless, since this is a *provisional* rejection, Applicants will address this issue upon the indication of allowable subject matter in this or the other application.

Applicants believe that all of the claims in the present application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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